

**REMARKS**

Applicants respectfully request entry of amendments to claims 12 and 16, and cancellation of claims 14 and 16-18. Support for the amendments can be found throughout the specification, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 12, 15, and 19 are in condition for allowance, or are in better condition for presentation on appeal, and respectfully request that the claims as amended be entered.

**Rejections Under 35 U.S.C. §112, First Paragraph**

Claims 12 and 14-19 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to enable one of skill in the art to make or use the invention. As claims 14 and 16-18 have been canceled, the rejection as applied to those claims is rendered moot. Applicants traverse the rejection as it might apply to the amended claims for the reasons given below.

The Office Action alleges, in pertinent part, that “the specification shows unpredictability for performing the method as broadly claimed.” (Office Action, page 5.) Without acquiescing to the reasoning offered by the Office, and in order to expedite prosecution of the instant application, Applicants have amended claim 12 to recite that the cell proliferative disorder is lung or head and neck cancer. Support for the amendment can be found in the specification as filed, in particular in Examples 7 and 8 (lung cancer), and Examples 5 and 8 (head and neck cancer).

The Office Action also alleges that the “specification has not provided guidance that the same truncated p16 gene is observed in any mammalian species and therefore it is unpredictable to correlated detection of any cell proliferative disorder in any species.” (Office Action, page 6.) Without acquiescing to the reasoning offered by the Office, and in order to expedite prosecution of the instant application, Applicants have amended claim 12 to recite the human p16 gene.

The Office Action alleges that the “claims are drawn to the detection of an absence of exon 1, which would include an absence in only one allele. The specification asserts, however, the detection of [Sic] homozygous deletion. Therefore there is no guidance for the detection of

hemizygous deletion as claimed.” (Office Action, pages 6-7.) Without acquiescing to the reasoning offered by the Office, and in order to expedite prosecution of the instant application, Applicants have amended claim 12 to recite that the truncated p16 gene product has a homozygous deletion of exon 1.

The Office Action alleges that the “specification indicates that the specific amplification of the entire exon 1 and 2 region is affected because the 5’ALT gene splices into the sequence and therefore the two specific primers used can not amplify the exon 1 region and the exon 2 region.” Applicants respectfully submit, however, that the exon 1 and 2 regions of the p16 sequence are not affected by the splicing of the 5’ALT gene into the **p15** gene. As detailed in the Specification, 5’ALT is 5’ of exon 2 of p15<sup>IN4B</sup>. (See, e.g., Figure 1b, Paragraphs [0012], [0019].) Therefore, since the 5’ALT gene does not splice into p16, but rather into p15, the exon1 and 2 region of p16 is not affected.

The Office Action also alleges that the “instant specification has not specifically defined truncated p16 gene” and “it is unclear if the truncated p16 gene only lacks exon 1 or if the truncated p16 gene encompasses the deletion of other regions.” (Office Action, page 7.) Without acquiescing to the reasoning offered by the Office, and in order to expedite prosecution of the instant application, Applicants have amended claim 12 to recite that the truncated p16 gene product has a homozygous deletion of exon 1.

Accordingly, withdrawal of the rejection is respectfully requested.

In re Application of:  
Sidransky and Baylin  
Application No.: 10/659,519  
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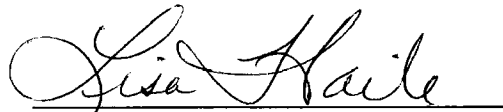
PATENT  
Attorney Docket No. JHU1300-6

**Conclusion**

Applicants submit that pending claims 12, 15 and 19 are in condition for allowance, or are in better condition for appeal. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

No fees are deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,



Lisa A. Haile, J.D., Ph.D.  
Registration No. 38,347  
Telephone: (858) 677-1456  
Facsimile: (858) 677-1465

Date: October 22, 2008

DLA Piper LLP (US)  
4365 Executive Drive, Suite 1100  
San Diego, CA 92121-2133  
**USPTO Customer Number 28213**